DETAILED ACTION

Applicants' arguments, filed 1/12/11, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 1-3, 13 and 17- 22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Spielberg C.A. in view of Sobel et al., Gillis et al. (all cited by examiner 10/12/2010) and Gennaro, Alfonso ("Remington's").

Applicant argues, contrary to assertions by the examiner in the previous Office action, that claims 1-3 and 13 recite ranges that are outside that taught by the art. Further, applicant argues none of the cited art teaches or suggests the possibility of lowering the dose of either active ingredients or the possibility of combining them in quantities that are not equivalent.

Examiner notes that even if claims 1-3 and 13 recite ranges that are outside the ranges taught by the prior art, they would have still been obvious over the previously cited prior art. The claimed ranges define concentrations of each agent which fall slightly below the amounts taught as effective by Sobel and Gillis. As stated in the prior Office action, however generally, differences in concentration will not support the

patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In this case, the combination of all the ingredients are suggested in the prior art, i.e., the general conditions are disclosed. The prior art shows that 150mg of fluconazole can treat candida infection and 2000 mg of tinidazole or 2000 mg of secnidazole can treat bacterial infection, clearly illustrating that the amount of these agents is result effective. The difference between the prior art and the current claims is the amounts disclosed for fluconazole, tnidazole, and secnidazole. Since there is no evidence of the criticality of these amounts, their differences from the prior art is not enough to render the claims patentable over the prior art.

Applicant argues lowering dosages of medicaments is counterintuitive if one wishes to cure a specific disease. Applicant further alleges lowering the doses is not recommended because, as a person skilled in the art would know, it would affect the treatment by possibly creating resistant microorganisms.

The examiner does not find these arguments persuasive as they are unsupported allegations by applicant.

Applicant argues the current invention provides a treatment that was still effective, even after lowering dosages, and thus reducing the possibility of adverse events. Thus, by lowering the dose of each active ingredient, the treatment provides an advantage over the prior art.

Examiner does not find this persuasive. It would appear that the patients referred to in the pharmacological examples in the specification at pages 19-22 were given dosages of fluconazole (112.5 mg) and tinidazole (1500 mg) twice a day, i.e., 225 mg fluconazole and 3000 mg tinidazole. It would appear that since the administered doses amounts are higher than the amounts claimed, then it is not critical to have less than 2000 mg tinidazole and less than 150mg fluconazole formulated in a tablet. Accordingly, the arguments are not persuasive.

Examiner submits that reducing the possibility of adverse events by lowering dosage amounts is not surprising. Indeed, it was already known that amounts of fluconazole can be lowered to amounts less than 150 mg while maintaining effectiveness for treating candidal infections and decreasing adverse effects. To rebut Applicant', suggestion that it is surprising that lowered dosage amounts of fluconazole maintained a level of efficacy, the Examiner cites Boedeker *et al* ("*Fluconazole dose recommendation in urinary tract infection."* Ann Pharmacother. 2001 Mar;35(3):369-72). Boedeker *et al* illustrated that fluconazole at a dosage of less than 150 mg maintains effectiveness by performing studies which lead them to the conclusion that a dosage of fluconazole of 200 md loading dose followed by 100 mg/d appears to be the most appropriate dose for the treatment of symptomatic candidal UTI in the patients. As such, dosage amounts less than 150 mg/d fluconazole was already known to maintain effectiveness; and the lower amount of the fluconazole would be expected to have reduced the possibility of side effects.

Claims 1, 13, 17, 19 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spielberg C.A in view of Sobel et al., Wallin et al. (cited by examiner 9/2/2009), and "Remington's".

Applicant notes that Wallin et al. teaches a dosage of tinadazole to be effective in quantities between 1.6g and 2g. Applicant asserts, however, Wallin et al. does not disclose the possible combination with another active ingredient.

The test of obviousness does not rest on whether a single reference expressly suggests the claimed invention. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. The combined teachings of the references would have suggested the invention as outlined in the previous Office action at pages 8 and 9. Accordingly, applicant's assertion is not found to be persuasive.

Applicant argues that although differences in concentration will not support the patentability of subject matter is true for concentrations falling within the ranges taught by the prior art, this does not hold true for concentrations falling outside the ranges taught by the prior art. Accordingly, applicant believes that claims 17, 19 and 21, as well as 1 and 13, each recite concentrations outside of the range taught by the prior art and, accordingly, are patentable.

The examiner does not find this argument to be persuasive. When concentrations fall within the ranges taught by the prior art, it is *prima facie* obvious and

when they fall outside the ranges taught in the prior art, they may still be found *prima facie* obvious as outlined in the MPEP at Section 2144.05.

Claims 2, 3, 18, 20, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spielberg C.A. in view of Sobel et al., Videau et al. (Cited in 09/02/2009 Office action), and "Remington's".

Applicant argues the examiner wrongly states that the claims recite the amounts of fluconazole and secnidazole to be within the amounts taught by the prior art. Because Applicant has specifically recited the dosages of the named ingredients as below that of the prior art, Applicant believes that such claims are allowable.

Examiner notes that even if claims 2, 3, 20 and 22 recite ranges that are outside the ranges taught by the prior art, they would have still been obvious over the previously cited prior art. The claimed ranges define concentrations of each agent which fall slightly below the amounts taught as effective by Sobel and Videau. As stated in the prior 10/12/2010 Office action at page 11, however generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In this case, the combination of all the ingredients are suggested in the prior art, i.e., the general conditions are disclosed. The prior art shows that 150mg of fluconazole can treat candida infection and 2000 mg of secnidazole can treat bacterial infection, clearly

illustrating that the amount of these agents is result effective. The difference between the prior art and the current claims is the amounts disclosed for fluconazole and secnidazole. Since there is no evidence of the criticality of these amounts, their differences from the prior art is not enough to render the claims patentable over the prior art.

Claims 6 and 16 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Spielberg C.A. in view of Sobel et al., Gillis et al., and "Remington's", the combination taken in view of USP 5,660,860 (previously cited 7/24/2008).

For reasons stated above applicant's assertion that the claims are allowable are not found to be persuasive.

Claim 16 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Spielberg C.A. in view of Sobel et al., Wallin et al., and "Remington's", the combination taken in view of USP 5,660,860.

For reasons stated above applicant's assertion that the claims are allowable are not found to be persuasive.

Claim 6 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Spielberg C.A. in view of Sobel et al., Videau et al., and "Remington's", the combination taken in view of USP 5,660,860.

For reasons stated above applicant's assertion that the claims are allowable are not found to be persuasive.

No claims are allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRIS SIMMONS whose telephone number is (571)272-9065. The examiner can normally be reached on Monday - Friday from 7:30 - 5:00 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/C. S./
Examiner, Art Unit 1612

/Patricia A Duffy/
Primary Examiner, Art Unit 1645